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DEPARTMENT OF BIOCHEMISTRY

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Dear Buzz:

I was shocked at the bad news your letter brought. Those of us that knew Raymond were much saddened by his death and although it cannot help Plana very much, everyone wanted to send their condolences. The tragedy for Marty Gellert must also have been staggering. Was she ill or did she have a history that made what happened likely? Since one's nervous system can only tolerate so much I can only wish that no more such "excitement" mars yours and Ann's year.

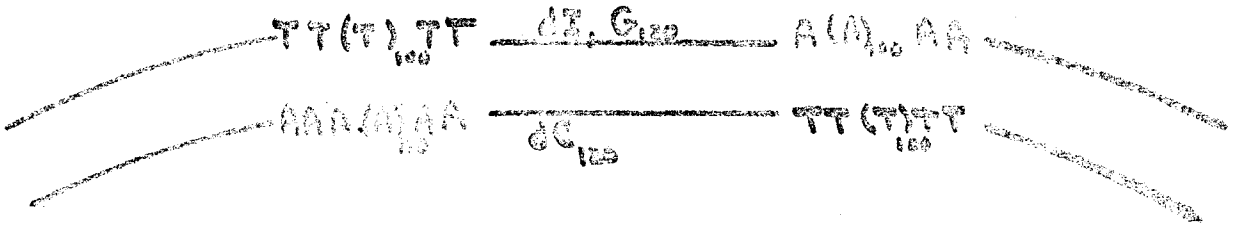
Buzz, at our last meeting we were trying to block out the graduate course schedule for the next few years. The following was what was confirmed:

	1971-72	1972-73	1973-74	1974
Fall		(Baldwin)	Hogness	
Winter		Lehman		
Spring	Shooter	Stark	Kaiser	Berg

I didn't know then what your plans were but since our meeting Scott told me that you had indicated to him that you were planning to teach (Proteins and Ultracentrifuge?) in the Fall of next year. Is that correct? That would be fine if it is. George's course is intended to be the continuation of Biochem. 200-201 (Enzyme Mechanism) and Bob Lehman could only teach in the Winter because of his heavy load in the Spring. Very likely Ron Davis will also teach in the Spring Quarter. If that scheduling is OK with you, Arthur will teach in the Fall or Winter of 1973-74 and Dave and Dale will fit their courses into the remaining quarters of that year.

I recently came across a paper in Nature by Stanley Bram (whose address is listed as the Pasteur Institut) on x-ray scattering experiments with poly dI:dC and poly dG:dC. Admittedly I'm not very expert in evaluating his data or even his interpretations but I could not miss his suggestion that the structure of these two polymers is "distinctly" different from that of the A or B form of DNA. I suspect he and probably you might have some idea of what type of structures one can imagine. If it is very "aberrant" it could bode ill for our attempt to use dI:dC as an insert into polyoma and SV40 DNA as

diagrammed below. We might be able to form the H-bonded structures whereby the dI, G:dC can bridge the ends of an SV40 molecule but can we ligase them. Note that the actual polymerase-ligase action should take place in the dA:dT "tails" region and maybe the dI:dC stretch need not ever see ligase. But clearly if it is triple-stranded or distorted in some way so as not to be accommodated in a covalently closed double-stranded circular molecule we would be in difficulty. And maybe that is our difficulty to date. Since you are our local expert on those structures any advice or intelligence you can offer would be appreciated.



Enclosed is a recent experiment using the S_1 nuclease to follow the annealing kinetics of P^{32}-labeled polyoma DNA. The enclosed protocol shows the annealing mixture and what it contained (the salmon sperm DNA is in to simulate the presence of cellular DNA when we do this with DNA from normal and infected (or transferred)cells. After heat denaturing, salt is added to 1.5 M and then the mixture is annealed at 68°. Samples (50µl) were taken at various intervals over 98 hrs (the mineral oil is essential to keep voline constant).diluted (6-fold) with the S_1 digestion buffer and frozen. When all samples collected, thawed and S_1 enzyme added and incubation for 60' at 37°. Samples acid-precipitated, filtered and counted. At zero time 4% of the P^{32} was acid-precipitable and this increased with time until at 98 hrs it was slightly greater than 80%. The red curve contained only P^{32}-PY DNA and the green curve was the same plus an equivalent amount of sheared cold PY DNA. The points and the curve define the computer generated best second-order curve based on all the experimental points (shown in crosses). As you can see the fit is good and as expected, the $Cot_{1/2}$ is halved! This is how we propose to search for or measure the amount of a particular sequence in a "sea" of different DNA.

Things are still humming along. Later this month we will be having our first 3-day departmental research meeting at Asilomar. Several groups will talk about their work and my hope is that by people rooming and eating together away from the lab we may get some more interesting discussion and thoughtful help from each other.

Scott and Barry seem to be getting along reasonably well. Barry says he hears from you regularly and since he seems to be working hard, I guess things are working out well for him. Scott, of course, is a gem and there's no concern for him. I've asked him to serve in your stead by taking over "supervision" of Carolyn Tate's activities since we shifted over to our "new" system.

I hope you were able to get the S_1 nuclease or its equivalent and that all goes well in the lab.

By the way, how did Gunther Stent's review (in the November Atlantic - see enclosed) of Jacque's book go over with Jacque? I expect we will soon see Gunther contemplating his navel while squatting on a bed of red hot coals or nails. In my next lecture on the genetic code, I shall have to also talk about the sixty-four elements of the I ching.

With best regards,

PB/l